

they would render the claimed invention obvious. The reference discloses ureas with bridged phenyl groups of formula (V) at col. 4, lines 10-15. The compounds of formula (V) contain phenyl substituted with R² and R³, which are alkyl, hydrogen nitro or halogen. The substituents R² and R³ of the reference are different than substituents on the ureas of this invention with bridged phenyl groups. The reference makes no mention of ureas with the bridged heteroaryl groups or bridged naphthyl groups of this invention.

With respect to the allegation regarding pKa differences over this reference, such is unfounded. Applicants never relied on the differences in pKa over this reference. The reference simply does not teach or suggests compounds that are claimed.

The Second Rejection Under 35 USC § 103

The Examiner also rejects the claims over Widdowson. The rejections over this reference are also unfounded.

The Examiner maintained the rejections over the compound claims even though the compounds of the claims have a pKa greater than 10, while the compounds of the reference have less than 10. The reference clearly teaches that the R₂ group has a functional moiety that provides an ionizable hydrogen having a pKa of 10 or less in the compound of formula Ib of the reference. See page 20, last two lines. One skilled in the art would not be motivated to eliminate such a group from the compounds of Widdowson, making the subject matter of the reference having no overlap with the claimed invention.

The Examiner would like to see unexpected results going from compounds of pKa of 10 to 11. This seems unreasonable and unsupported by law and facts and/or sound reasoning. Once a *prima facie* case of obviousness is established, which is not done here, and is not admitted, the applicant can go forward with rebuttal evidence. Because the presently claimed invention is not obvious for the reasons discussed above and below, the necessity to submit a declaration to overcome the rejections is not present.

The allegation more specifically is that one experimenting with the reference would have obtained compounds with pKa of 9 or 11. However, there is no support for such an allegation. Nothing in the reference teaches or suggests to one of ordinary skill in the art to even try to achieve compounds of formula Ib therein having pKa values at or near the maximum of the limit

disclosed by the reference. The reference merely provides a very broad teaching which does not even overlap the claimed subject matter. Additionally, the reference does not teach a single species of the formula Ib. All the compounds prepared in the reference are of formulae over which no rejections are made, which are farther from the claimed invention herein.

Additionally, the cases are clear that unexpected results have to be demonstrated over the closest prior art. See *In re De Blauwe*, 736 F.2d 699, 705, 222 USPQ 191 (Fed. Cir. 1984), and *In re Merchant*, 575 F.2d 865, 869, 197 USPQ 785 (CCPA 1978). Here the closest prior art is a broad general formula in the reference, which does not overlap the claimed invention, and of which not a single species is prepared in the prior art to which applicants can compare the compounds of the claimed invention. Nothing in the law requires applicants to prepare compounds not taught or suggested by the reference and compare the same to their own invention.

Additionally, the rejection over independent claim 27 is unfounded. The Examiner is stating that position isomers are prima facie obvious as a whole while citing *Ex parte Mowry*, 92 USPQ 219 (POBA 1950). Applicants point to *Ex parte Mowry and Seymour*, 91 USPQ 219 (BPAI 1951), which restricted the holding of *Mowry* relied on by the Examiner, where a cyclohexyl group was substituted in a different position than in the prior art (more similar situation to the present case where L¹ is a cyclic group). The Board in the latter case held that position isomers that could be considered obvious over each other have properties that are often so nearly alike as to present difficulties in identification or in separation in mixtures thereof. The holding of obviousness in *Mowry and Seymour* was reversed. The compounds of Claim 27 are structurally different from the reference's formula and are not merely obvious isomers thereof.

The Examiner also alleges that the reference teaches the treatment of cancer. Applicants respectfully disagree. Nowhere in the reference does the term "cancer" appear. The Examiner points to page 89, line 25, of the reference, which states that "the α -chemokines ... working through the IL-8 type I or II receptor can promote the neovascularization of tumors by promoting the directional growth of endothelial cells. Therefore, the inhibition of IL-8 induced chemotaxis or activation would lead to a direct reduction in the neutrophil infiltration." This material however does not teach or suggest the treatment of cancer (note that the term "cancer" is never mentioned), and the PTO has not established that one of ordinary skill in the art would

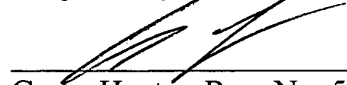
understand the quoted material to teach the treatment of cancer.

Additionally the reference on the very same page referred to by the Office Action provides a laundry list of diseases by name that are associated with IL-8, and cancer is not one of them. See page 89, lines 8-15. The reference on page 89, line 17, states that "these diseases (language following the laundry list of diseases, which list does not contain cancer) are primarily characterized by massive neutrophil infiltration." The quoted language from the examiner refers to achieving "reduction in the neutrophil infiltration." Accordingly, one of ordinary skill in the art would understand the quoted language referred to by the PTO to be associated with the diseases in the list provided on that same page, and not with cancer.

Reconsideration is respectfully requested.

The Commissioner is hereby authorized to charge any fees associated with this response or credit any overpayment to Deposit Account No. 13-3402.

Respectfully submitted,



Csaba Henter, Reg. No. 50,908
Richard J. Traverso, Reg. No. 30,595
Attorney/Agents for Applicant(s)

MILLEN, WHITE, ZELANO
& BRANIGAN, P.C.
Arlington Courthouse Plaza 1, Suite 1400
2200 Clarendon Boulevard
Arlington, Virginia 22201
Telephone: (703) 243-6333
Facsimile: (703) 243-6410

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